IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Jay A. Goldstein, Michael Rothman, and Whe-Yong Lo		
Serial No.:	10/691,928	Art Unit:	1616
Filed:	October 23, 2003	Examiner:	David Paul Stitzel
For:	*ANTIFUNGAL FORMULATIONS*		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

I, Jay A. Goldstein, hereby declare that:

1. I am a co-inventor of the above-identified application. I have been a licensed physician since July 1973. I began my medical career as an Emergency Physician, and practiced this specialty for four years. In September of 1977, I started training in Dermatology, and became a fully trained Board Certified Dermatologist in November of 1980. My CV is attached as Exhibit A.

2. During my long medical career, both as an Emergency Physician, and as a Dermatologist, I have found that rashes, and particularly inflammatory tinea (ringworm) were a particularly common and often stubborn problem to treat. Such rashes respond to topical anti-fungals, but in a very slow fashion. It can take up to 4-6 weeks for these rashes to clear and for the patient to be symptom free. Even as the rash fades, the patient is still often bothered by

intense, unremitting itching, burning and discomfort. There was, and is a product, Lotrisone, which was developed to both treat the tinea, as well as the accompanying inflammation and itching, which were often the main reasons that the patient sought medical attention. Lotrisone was a combination of anti-fungal clotrimazole with a high potency corticosteroid, betamethasone dipropionate. This drug was effective in clearing the tinea, as well as rapidly decreasing the itching, which without the steroid, would normally last up to several weeks. With Lotrisone, however, the itching component would often disappear within days, making the patient more comfortable. The problem with Lotrisone, however, was that the steroid was too potent to be used safely on thin skinned area of the body, and thus often caused stretch marks, thinning of the skin, as well as other changes.

3. Because of my many years of experience both as an Emergency Room Physician, and as a Dermatologist, I saw the need for a preparation which would address both the fungal infection, as well as the intense itching and inflammation associated with the fungal infection. While others thought that perhaps slightly lower potency or even higher potency steroids would be acceptable, I felt that any steroid other than those safe for use on the face and other thin skinned area would not be appropriate. Of course, there was the risk that lower potency steroids would not be effective. I began using anti-fungal preparations in conjunction with low potency topical steroids on my patients with inflammatory tinea, and found that in fact such preparations were both safe and effective. They shortened the time to clearing of the fungus, and they dramatically decreased the symptoms of redness and especially itching. It would have been

unethical to compare the type of products that I used with compounds using stronger, more potent steroids, as there would be the real risk of major untoward side effects.

4. I have developed a formulation that that rapidly clears both their fungus, and their associated symptoms of itching and inflammation. This is further demonstrated by studies conducted using topical compositions containing a combination of an antifungal agent in combination with a low to mid potency anti-inflammatory steroid in the treatment of fungal diseases and their related inflammation, especially for conditions such as tinea cruris, intertriginous dermatitis, and tinea corporis.

5. Case Report

Patient: C.S, 74 y.o. White male

History of Present Illness: Long standing recurrent tinea cruris of inguinal folds.

Initial Treatment: None

Physical Examination: Erythema with scale in inguinal folds.

Diagnosis: Tinea Cruris

Treatment: Clotrimazole 1% cream with alclometasone dipropionate 0.05% cream applied twice daily.

Results: Complete clearing after several weeks of usage.

6. Case Report

Patient: B.T. 72 y.o. White female

History of Present Illness: Several days of pruritic inflamed eruption beneath right breast.

Prior Treatment: None

Physical Examination: Erythematous dermatitis beneath right breast.

Diagnosis: Intertriginous Dermatitis.

Treatment: Oxicanozole cream 1% with Hydrocortisone cream 2½% applied twice daily.

Results: Marked clearing at seven days.

7. Case Report

Patient: D.E. 52 y.o. White male.

History of Present Illness: Two months of very pruritic eruption beginning on left foot, spreading to right hand.

Initial Treatment: None

Physical Examination: Well-defined, annular, scaly, erythematous, inflamed eruption on dorsum surface left foot, with similar plaque on right hand.

Diagnosis: Tinea Corporis

Treatment: Econazole cream 1% with fluocinalone acetonide cream 0.01% applied twice daily.

Results: Marked decrease of pruritus within 3 days. Eruption essentially cleared at 3 weeks.

8. Case Report

Patient: M.B. 61 y.o. White male

History of Present Illness: Eruption of right and lower leg of several months duration. Known history of "tinea."

Prior Treatment: None

Physical Examination: Plaques of annular dermatitis of lower legs, right greater than left. 10 toenail onychomycosis.

Diagnosis: Tinea corporis, with tinea pedis and onychomycosis.

Treatment: Econazole cream 1% with alclometasone dipropionate 0.05%, applied twice daily.

Results: Marked clearing at 3 weeks, but with some residual eczematous changes still present.

9. Case Report

Patient: R.B. 62-year old white male.

History of Present Illness. Eruption began on right lower leg in mid-August. No response to topical steroids.

Physical Examination: Raised annular eruption on right lower leg.

Laboratory. Biopsy on September 26, 2005 revealed hypersensitivity reaction.

Additional Treatment. High potency steroids again prescribed without effect.

Additional laboratory Test. Special stains revealed inflammatory tinea.

Treatment: Application twice daily of desonide cream and clotrimazole cream together resulted in essentially complete clearing within two weeks.

10. In summary, oxicanozole cream 1% with hydrocortisone cream 2½% applied twice daily and econazole cream 1% with fluocinalone acetonide cream 0.01% applied twice daily resulted in marked clearing of pruritus and the eruption at 3 weeks. Clotrimazole 1% cream with acalmetasone dipropionate 0.05% cream applied twice daily was effective in completely clearing long standing recurrent tinea cruris, after several weeks of usage. Econazole cream 1% with alclometasone dipropionate 0.05% applied twice daily resulted in marked clearing of eruption in a patient with a history of tinea.

11. Enclosed with this declaration are colored photographs showing bright red erythematous eruptions on a patient's leg before treatment (labelled "Before Treatment") and the patients leg after treatment with desonide cream and clotrimazole cream (labelled "After Treatment") along with the patient record (Exhibit D). No response had been obtained with topical steroids. Upon initial examination of the patient, high potency steroids were again prescribed without effect. Application of a combination of desonide cream and clotrimazole cream (twice daily) resulted in marked improvement in five days and essentially complete clearing within two weeks.

12. The compositions used in the examples above have advantages over other compositions which contain very potent steroids such as betamethasone and dexamethasone (see Goodman and Gilman's The pharmacological Basis of therapeutics, 9th edition, 1996, p1466, attached as exhibit B) associated with severe side effects. It is undesirable to use mid-potency or higher potency steroids for topical treatment for extended periods of time because of associated risks. The compositions exemplified above employ low potency, Class 6 steroids (see attached (Exhibit C) potency chart of steroids listed by the National Psoriasis Foundation), i.e. fluocinalone acetonide, alclometasone dipropionate, desonide, and hydrocortisone 2 ½%. Other commercialized products have utilized only 1% hydrocortisone, which is too low in potency to have significant anti-inflammatory properties. We utilize prescription strength steroids that are safe for all parts of the skin, are safe for extended periods of use, but have superior potency as compared to OTC products.

13. I declare that all statements made herein of my own knowledge and belief are true and that all statements made on information and belief are believed to be true, and further, that the statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 2/26/07

Jay A. Goldstein

EXHIBIT A

U.S.S.N. 10/691,928
Filed: October 23, 2003
DECLARATION UNDER 37 C.F.R. § 1.132

Curriculum Vitae

Identifying Information	Jay A. Goldstein, M.D. 31 Claremont Street Newton, Massachusetts 02158
Office Address	67 Union Street – Suite 501 Natick, Massachusetts 01760
Date and Place of Birth	January 9, 1947 Paterson, New Jersey
Citizenship	U.S.A.
Pre-medical Education	Boston University School of Medicine 1968 – 1972 M.D., 1972
Internship	Herrick Memorial Hospital Berkeley, California 1972 –1973 Rotating
Residency	Boston University Medical Center Dermatology 1977 – 1980
Licensure	Massachusetts #39484 Rhode Island #9865
Certification	American Board of Dermatology, 1980
Professional Societies	American Academy of Dermatology Society of Investigative Dermatology
Academic Appointments	Boston University School of Medicine, Associate in Dermatology
Hospital Appointments	Metrowest Medical Center Natick, Massachusetts Boston Medical Center Boston, Massachusetts
Publications	1. Goldstein JA and Pochi PE: Failure of Benzoyl Peroxide to Decrease Sebaceous Gland Secretion in Acne Dermatologica 162: 287-291, 1981

Curriculum Vitae

2. Shalita AR, Strauss JS: Comparative Effect of Isotretinoin and Etretinate on Acne and Sebaceous Gland Secretion. Journal of the American Academy of Dermatology 6: 760-765, 1982

3. Goldstein JA, Comite H, Mescon H, Pochi PE: Isotretinoin in the Treatment of Acne: Histologic Changes, Sebum Production, and Clinical Observations. Archives of Dermatology 118: 555-562, 1980

4. Goldstein JA, Pochi PE: Adolescent Acne. The Female Patient 5: 57-66, 1980

5. Barza M, Goldstein J, Kane A, Feingold DS, Pochi, P: Systemic Absorption of Clindamycin Hydrochloride After Topical Application. Journal Amer Acad Dermatol 7: 208-14, 1982